

FACTSHEET

SPONSORED BY



REGENERATIVE MEDICINE

BY STACEY OKE, DVM, MSC; REVIEWED BY ASHLEE WATTS, DVM, PHD, DIPL. ACVS

REGENERATIVE MEDICINE USE IN HORSES

Scientific advances culminating in the birth of regenerative therapies can help horses recover following injury

t one point or another, most athletic horses suffer some type of musculoskeletal injury, regardless of their performance level. Joints, tendons, and ligaments are among the most commonly affected structures.

In joint injury/disease for example, once the joint becomes inflamed, a series of events results in continued inflammation, culminating in pain, swelling, decreased range of motion, and a progressive deterioration of the articular cartilage lining the ends of long bones.

Tendons and ligaments, on the other hand, do attempt to heal, but instead of simply repairing or replacing injured fibers, the body produces scar tissue. Scar tissue has far less strength and elasticity than normal, healthy tendon and ligament fibers, which explains why tendon and ligament reinjury rates are so high despite prolonged recovery times (six to nine months or more).

Veterinarians use a variety of diagnostic tools to identify these injuries, including but not limited to physical exams and flexion tests, needle arthroscopy, MRI, X ray, and ultrasound. An accurate diagnosis can help veterinarians identify an appropriate treatment plan.

Treatment options vary greatly and can include rehabilitation, medical, shoeing, and surgical techniques.¹ Of the many available treatment options, three — stem cell therapy, interleukin-1 receptor antagonist protein therapy (IRAP), and platelet-rich plasma (PRP) — fall into a unique class of therapies called "regenerative medicine." As defined by the National Institutes of Health, "regenerative medicine is the process of creating living, functional tissues to repair or replace tissue or organ function lost due to age, disease, damage, or congenital defects."²

The concept is to help the body repair injured tissues with its own cells to maximize healing.

STEM CELL THERAPY

Stem cell therapy appears to be a highly valuable tool for managing musculoskeletal injuries. Stem cells can be "coaxed" into becoming tissue-specific cell types, such as tendons and ligaments. Common stem cell sources include adipose (fat) tissue, bone marrow, fetal tissues, and even dental pulp. Stem cells from adipose tissue can be concentrated and separated from other tissue components before being injected back into the patient. While this approach results in only a very small percentage of actual stem cells being administered, they can often be injected very soon after an injury has been diagnosed.

Mesenchymal stem cells (MSCs), derived from bone marrow, can also be collected, concentrated, and injected relatively rapidly; however, researchers recommend using stem cells obtained from bone marrow (or even fat) that have been sent to a laboratory and grown in cultures to produce millions of cells. Those culture-enhanced stem cells take two to four weeks to prepare. Once they've been produced, veterinarians can inject about 10 million cells into the lesion under ultrasonic guidance. Injections can be repeated every four weeks for three to four treatments. That said, optimal dosing and treatment intervals remain unknown.³

Researchers have found that the stifle appears to be the joint most amenable to stem cell therapy, especially for cases associated with meniscal and soft-tissue injuries. Veterinarians can inject approximately 10-20 million stem cells per joint. Again, exact dosing has not been fully established.⁴

IRAP THERAPY

IRAP continues to gain traction in the realm of joint disease treatments.⁴ This regenerative therapy, also called autologous conditioned serum (ACS, autologous means self-derived), can be produced using samples from the horse's own body. Veterinarians collect a small volume of blood from the patient and allow it to clot. Then, they mix the serum—the liquid portion of blood that separates from red blood cells—with special borosilicate glass beads included in commercial ACS kits. This produces anti-inflammatory molecules

called interleukin-1 receptor protein agonists, which block the action of interleukin-1, a very potent pro-inflammatory molecule. Veterinarians inject the "conditioned" serum directly into the affected joint(s) to exert this anti-inflammatory effect. Additional growth factors produced during the incubation process that can help with healing include interleukin-10, fibroblast growth factor, vascular endothelial growth factor, and platelet-derived growth factor, among others.³ The conditioned serum takes about 24 hours to produce.

One recent review confirmed that horses with experimentally induced osteoarthritis treated with IRAP had a significant improvement in lameness and healing.

Treatment protocols vary, but injecting 2-10 mL of conditioned

serum (depending on the size/volume of the joint) into the affected joint every three to 10 days, for a total of three treatments, appears effective.⁴ For long-term maintenance of chronic joint disease, a single injection of IRAP administered on an as-needed basis appears effective. IRAP/ACS injections can, like any



Veterinarians use stem cell injections to treat a variety of musculoskeletal ailments in horses.

WHAT IS REGENERATIVE MEDICINE?

joint injection, cause a "joint flare," associated with heat, pain, and lameness.

Some practitioners use IRAP to treat soft-tissue injuries; however, no scientific studies have been conducted supporting this application.³

PRP

Platelets are specific types of blood cells that naturally contain a rich array of growth factors. Veterinarians can generate PRP using a commercial system that separates the platelets from other blood components, such as red and white blood cells, and concentrates them into an easily injectable product.5 Like IRAP, collecting a patient's blood and using it to produce PRP makes this an autologous process, where the body's tissues heal itself.

Despite minimal research in this field, many sport horse practitioners report positive results after injecting PRP directly into injured joints.⁴ Based on the available data, between 2 and 6 mL of prepared PRP can be injected per joint. As with IRAP/ACS, post-injection flares can occur.⁴

The more widely accepted and studied—use is in managing soft-tissue injuries. PRP appears to promote tissue healing (rather than laying down scar tissue), resulting in tendons and ligaments with improved strength and elasticity compared to untreated horses.

In turn, horses have a reduced risk of reinjury. Once a veterinarian diagnoses a tendon or ligament lesion, PRP produced using a stallside kit can be injected directly into the defect using an ultrasound-guided or needle arthroscope approach. The "fresher" the lesion the better, and injections can be repeated every three to four weeks.³

FUTURE DIRECTIONS IN REGENERATIVE THERAPY

Still well within its infancy, regenerative medicine holds much promise in managing common musculoskeletal injuries.

Now, as veterinarians and researchers become more comfortable with these

Resources

- Wilson JM1, McKenzie E, Duesterdieck-Zellmer K. International survey regarding the use of rehabilitation modalities in horses. Frontiers in Veterinary Science. 201811;5:120.
- U.S. Department of Health and Human Services. National Institutes of Health. report.nih.gov/ nihfactsheets/ViewFactSheet.aspx?csid=62.
- Ortved KF. Regenerative medicine and rehabilitation for tendinous and ligamentous injuries in sport horses. Veterinary Clinics of North America Equine Practice. 2018;34(2):359-373.
- Contino EK. Management and Rehabilitation of Joint Disease in Sport Horses. Veterinary Clinics of North America Equine Practice. 2018;34(2):345-358.
- Oke S. Platelet-rich plasma. The Horse. 2011. Available at: s3.us-east-2.amazonaws.com/ thehorse/files/V/platelet-rich-plasma.pdf.
- Marycz K, Michalak I, Kornicka K. Advanced nutritional and stem cells approaches to prevent equine metabolic syndrome. Research in Veterinary Science. 2018;118:115-125.
- Angelone M, Conti V, Biacca C, et al. The contribution of adipose tissue-derived mesenchymal stem cells and platelet-rich plasma to the treatment of chronic equine laminitis: a proof of concept. International Journal of Molecular Science. 2017;18(10). pii: E2122

This Fact Sheet may be reprinted and distributed in this exact form for educational purposes only in print or electronically. It may not be used for commercial purposes in print or electronically or republished on a Web site, forum, or blog. For more horse health information on this and other topics visit TheHorse.com. Published by The Horse: Your Guide To Equine Health Care, © Copyright 2018 The Horse Media Group. Contact editorial@TheHorse.com.

Conclusive Micro-Invasive Stifle Lameness Diagnostics on CONSCIOUS Horses plus Stem Cells for Regenerative Therapy of Damaged Joints



NeedleView[™] Arthroscope: Better By Any Measure

- Utility: 1.2mm diameter (18 gauge) arthroscope is ideal for diagnosis, wait-and-watch, pre-op, and post-surgery/ post-treatment second looks
- Procedure cost: Much lower than standard arthroscopy
- Transport: Not required; can be done in wash rack, trailer, etc.
- General anesthesia: Not required; use sedation and local block

The ONLY non-surgical modality for conclusive diagnosis of meniscal tears and lesions, cartilage damage, cruciate ligament tears and lesions, floating joint fragments, and subchondral cysts.





Visit biovisionvet.com/products/needleview-arthroscope-suite/ for more information or call Biovision at 303-225-0960.



Advanced Regenerative Therapies (ART): Trusted Scientific Provider of State-of-the-ART Regenerative Medicine to the Veterinary Community

- · Peer-to-peer consultation on cases
- Bone marrow-derived stem cell expansion and banking
- Overnight shipping available for the U.S., Canada, and Mexico

In the Ferris et al. 2009 trial, 77% of the horses treated were able to go back to work after failing other medical treatment. This represents a 2.5x improvement of the most severe meniscal lesions over surgery alone.





Visit art4dvm.com for more information or call ART at 970-212-0749.

Stem cells are being studied for use in horses with laminitis and even in the management of equine metabolic syndrome.^{6,7} Additional research, especially in the realm of stem cells, to create optimal treatment protocols and identify

techniques, exploration of novel

uses of stem cells is increasing.

appropriate combinations with other regenerative and rehabilitation therapies to maximize efficacy, remains a leading area of focus.